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10/584,982	04/02/2007	Robin Kurfurst	15675P620	2408

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Blakely, Sokoloff, Taylor & Zafman
12400 Wilshire Boulevard, 7th floor
Los Angeles, CA 90025

EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,982	KURFURST ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-57* is/are pending in the application.

4a) Of the above claim(s) *22-37 and 39-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 42-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *November 20, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Election filed December 18, 2007.

Claim 38 has been amended. New claims 42-57 are acknowledged.

Claims 22-57 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group VI, drawn to a method for depigmenting or bleaching human skin, body hair and/or head of head comprising administering a cosmetic or topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1, wherein the oligonucleotide comprises SEQ ID NO:1, in the reply filed on December 18, 2007 is acknowledged.

The traversal is on the ground(s) that the restriction required by the Examiner concerning a selection of a particular sequence comprised by the oligonucleotide specific for PKC beta-1 is improper since all sequences have in common being specific for PKC beta-1.

This traversal has been considered, but is not found persuasive because although the oligonucleotides used in the methods are each specific for PKC beta-1 and are therefore commonly specific for PKC beta-1, each of the oligonucleotides specific for PKC beta-1 is structurally and functionally independent and distinct because they have very different nucleotide sequences (see Applicant's specification at Table 1, page 20). Furthermore, each of the oligonucleotides specific for PKC beta-1 used in the

methods as claimed targets a different and specific region of PKC beta-1 (see Applicant's specification at Table 1, page 20). In this regard, restriction as indicated is proper since each of the oligonucleotides specific for PKC beta-1 used in the methods as claimed would require a different field of search (for example, employing different search queries).

Claims 22-37 and 39-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Additionally, SEQ ID NOs: 2-5 as recited in claim 43 and SEQ ID NO:4 as recited in claim 44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **with** traverse in the reply filed on December 18, 2007.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 38 and 42-57 have been examined on the merits.

Information Disclosure Statement

Applicant's information disclosure statements filed November 20, 2006 are acknowledged. The submissions are in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statements, and signed copies are enclosed herewith.

Specification

Applicant's reference to priority in the first sentence of the specification is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38, 42, and 46-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 38, 42, and 46-56 are drawn to a method for depigmenting or bleaching human skin, body hair and/or head of head comprising administering a cosmetic or topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. Claim 57 is drawn to a method for the treatment or the prevention of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the

treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1.

The specification teaches protein kinase C with GenBank Accession No. X06318. A brief review of the prior teaches protein kinase C with GenBank Accession Nos: M19007; NM_212535; NM_002738; NM_009955; and NM_012713, for example. The prior art also teaches antisense oligonucleotides targeted to human protein kinase C-beta 1 (see Lazou et al., Journal of Drugs in Dermatology, 2007 Vol. 6:s2-27). However, neither the instant specification, nor the prior art describe oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1, other than the above sequences listed.

At the outset, it is noted that the rejected claims do not recite any sequence identifier relating to protein kinase C beta-1. This sequence is thus considered to be defined by its function (i.e. the activity of protein kinase C beta-1) rather than by any one specific structure. Accordingly, the claims embrace methods of using oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1, or any such molecule with analogous protein kinase C beta-1 activity, known or yet to be discovered, along with any isoform or allele present within this species, or any variant, polymorphic or otherwise, that is within reasonable similarity from these families of proteins that retain protein kinase C beta-1 activity.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in

the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof. The representative sample requirement may be satisfied by supplying structural or functional information, or a combination of both, such that one of skill in the art would be satisfied that applicants were in possession of the genus as claimed. Further, the size of the representative sample required is an inverse function of the unpredictability of the art.

See the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement. These guidelines state: "[T]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including

description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention.

Further, See MPEP § 2163, which states "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

In order to synthesize the oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 and to practice the methods claimed, one of skill would first need the sequence of the protein kinase C beta-1. Although the instant specification and the prior art teaches a series of target sequences for protein kinase C beta-1, the claimed methods of using oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 are directed to *any* sequence of *any* protein kinase C beta-1, or any such molecule with analogous protein kinase C beta-1, activity, known or yet to be discovered, along with any isoform or allele present within this species, or any variant, polymorphic or otherwise, that is within reasonable similarity from these families of proteins that retain protein kinase C beta-1, activity. Apart from further experimentation, the skilled artisan would not have been able to predict the structures of the full scope of the claimed

oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 encompassed by the instant invention, particularly in the absence of any teaching by way of structure or reference to active domains or regions. The genus is not immediately envisioned because the genus of oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 is considered to include not only the protein kinase C beta-1 sequences taught in the instant invention and the prior art, but also any such molecule with analogous protein kinase C beta-1 activity, known or yet to be discovered. However, the distinguishing characteristics of the claimed genus are not considered to be described herein, or in the prior art. Thus, because one of skill in the art could not envision any oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1, one of skill would not be convinced that Applicants were in possession of any oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 is considered to include not only the protein kinase C beta-1 sequences that are heretofore undescribed.

******

Claim 57 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the **treatment** of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the

treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1, does not reasonably provide enablement for a method for the **prevention** of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to made and/or use the invention commensurate in scope with these claims. This is a scope enablement rejection.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art,

and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

Claim 57 is drawn to a method for the treatment or the prevention of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. The nature of the invention, therefore, requires the knowledge of using oligonucleotide molecules that can be delivered to cells or tissues in a subject (*in vivo*) such that regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing and treatment of certain leucodermias such as vitiligo is treated or prevented.

The amount of direction or guidance and presence/absence of working examples:

Applicants disclosure and the prior art teach a method of modulating the expression of PKC-beta 1 and a method of treating a condition associated with the expression of PKC-beta 1 comprising the topical administration to a mammal an oligonucleotide said oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA (see Applicant's specification and WO 95/02069 A1 ('069) (submitted and

made of record on Applicant's Information Disclosure Statement filed November 20, 2006). However, neither Applicants nor the prior art has shown a method for the *prevention* of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. Applicant has not shown that any condition listed in claim 57 could be *prevented.* In addition, the Applicant does not disclose how the oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 are to be used in order to *prevent* a condition listed in claim 57. It is not clear from the specification, that in order for *prevention* of a condition associated with protein kinase C beta-1, such as those listed in claim 57, whether the patient is potentially prone for such condition or whether a recurrence is being prevented. Is the therapy to *prevent* recited here started months ahead or days ahead of a probable expectation of developing a condition associated with protein kinase C beta-1, such as those listed in claim 57? Is there a particular amount of the formulation that needs to be administered? Is a particular treatment regimen necessary? How long must such a treatment continue in order to *prevent* a condition associated with protein kinase C beta-1, such as those listed in claim 57?

<u>The state of the prior art and the predictability or unpredictability of the art:</u>

The claimed invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001). The claims encompass a method for the treatment or the prevention of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. However, the specification and the prior art only show a method of treatment, not a method of prevention.

The level of skill in the art:

The level of skill in pertinent art is considered to be high, being a graduate student or post-doctoral fellow in a biological science.

The quantity of experimentation necessary:

The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of how to devise a method for the prevention of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the treatment of certain leucodermias such as vitiligo, comprising the topical

application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. As neither the prior art nor the specification provide guidance as to how to *prevent* protein kinase C beta-1 associated diseases, such analysis is replete with trial and error experimentation. Such experimentation represents an inventive and unpredictable undertaking in itself, with each of the many intervening steps, not providing any guarantee of success.

In order to practice the invention as claimed, one would first have to successfully devise a method for the prevention of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. Due to the broadness of the claims, one of skill in the art would be required to further undertake extensive trial and error experimentation with a large number of subjects and controls to determine how to successfully *prevent* any condition listed in claim 57.

Thus, given the broad claims in an art whose nature is identified as unpredictable, the state of the prior art, the lack of guidance in the specification, the breadth of the claims and the quantity of experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention

commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38 and 42-57 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/02069 A1 ('069) (submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006) as evidenced by Lazou et al. (Journal of Drugs in Dermatology, 2007 Vol. 6:s2-27).

Claim 38 is drawn to a method for depigmenting or bleaching human skin, body hair and/or head of head comprising administering a cosmetic or topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1. Claims 42-56 are dependent on claim 1 and include all the limitations of claim 1 with the further limitations wherein said composition comprises at least one oligonucleotide capable of specifically hybridizing with any 5' to 3' regions, coding or non-coding region of genes coding for PKC beta-1; wherein said composition comprises SEQ ID NO:1; wherein said composition comprises chemical modifications including modified sugar moieties of 2'-O-fluoro substituents; wherein said composition comprises a phosphodiester groups; wherein the phosphodiester groups are replaced by phosphorothioate groups; wherein

the phosphodiester groups are replaced by methylphosphonate groups; wherein said composition comprises a vector or plasmid; wherein said composition comprises one or more active agents, including anti-inflammatory agents; wherein the oligonucleotide represents 0.00001% to 10% of the total weight of the composition; and wherein said composition is presented in the form of an emulsion containing an oil. Claim 57 is drawn to a method for the treatment or the prevention of regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing, and for the treatment of certain leucodermias such as vitiligo, comprising the topical application of a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1.

'069 discloses and claims a method of modulating the expression of PKC-beta in cells comprising contacting the cells with an oligonucleotide said oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA (see claims 37 and 44, 45, and 48). '069 discloses that the oligonucleotide is specifically hybridizable with a 5' untranslated region, coding region or 3' untranslated region (see claim 38). '069 also discloses that the oligonucleotide comprises intersugar linkages, including a phosphorothioate moiety (see claim 39). '069 also discloses that the oligonucleotide comprises a 2'-fluoro modification or a 2'-O-methyl modification (see claims 41 and 42). '069 also discloses and claims that the oligonucleotide is SEQ ID NO:28, where SEQ ID NO:28 is identical to SEQ ID NO:1 of Applicant's invention (see claim 49). '069 also

discloses and claims a method of treating a condition associated with the expression of PKC-beta comprising administering to a mammal an oligonucleotide said oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA, wherein the condition is a hyperproliferative disorder, including psoriasis or skin cancer (see claims 70-72, 76, 86, and 89). '069 discloses that the oligonucleotide is specifically hybridizable with a 5' untranslated region, coding region or 3' untranslated region (see claim 77). '069 also discloses that the oligonucleotide comprises intersugar linkages, including a phosphorothioate moiety (see claim 78). '069 also discloses that the oligonucleotide comprises a 2'-fluoro modification or a 2'-O-methyl modification (see claims 80 and 81). '069 also discloses and claims that the oligonucleotide is SEQ ID NO:28, where SEQ ID NO:28 is identical to SEQ ID NO:1 of Applicant's invention (see claim 90). '069 also discloses that the oligonucleotide compositions also include active ingredients such as anti-inflammatory agents (see page 18, lines 1-3) and oily based emulsifiers (see page 18, lines 14-24). '069 also discloses and claims that the oligonucleotide compositions of their invention are pharmaceutical compositions comprised in a pharmaceutically acceptable carrier (see claim 18) and are administered topically (see page 18, lines 6-13).

It is noted that '069 is silent as to whether or not their method of modulating the expression of PKC-beta in cells or method of treating a condition associated with the expression of PKC-beta comprising administering to a mammal an oligonucleotide said oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA, wherein the condition is a hyperproliferative disorder, including psoriasis or skin cancer

specifically depigments or bleaches human skin. However, it is the Examiner's position that the topical administration to the skin of an oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA as disclosed by '069 would inherently depigment or bleach human skin, as evidenced by Lazou et al. who teach that the topical administration of antisense oligonucleotides targeted to PKC-beta 1 lightens and whitens skin (see Abstract and Table 1). Therefore, absent evidence to the contrary, the topical administration to the skin of an oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA as disclosed by '069 would inherently depigment or bleach human skin.

It is further noted that '069 is silent as to whether or not their method of modulating the expression of PKC-beta in cells or method of treating a condition associated with the expression of PKC-beta comprising administering to a mammal an oligonucleotide said oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA, wherein the condition is a hyperproliferative disorder, including psoriasis or skin cancer *specifically* treats regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing or treats certain leucodermias such as vitiligo. However, it is the Examiner's position that the topical administration to the skin of an oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA as disclosed by '069 would inherently treat regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign

melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing or treat certain leucodermias, absent evidence to the contrary.

The burden of establishing whether the prior art method has the function of treating regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing or treating certain leucodermias, under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence

that the that the topical administration to the skin of an oligonucleotide being specifically hybridizable with a PKC gene or PKC mRNA as disclosed by '069 would or would not have the additional functional limitation of treating regional hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing or treating certain leucodermias as instantly claimed.

Therefore, absent evidence to the contrary, claims 38 and 42-57 are anticipated by WO 95/02069 A1 as evidenced by Lazou et al.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information

for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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>
> For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

tcg
January 26, 2008

/Terra Cotta Gibbs/